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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,580	10/06/2003	Usha Kasid	GTU-06-1134WO-US	8237

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,580	KASID ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4, 5 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 12/04/2006, and a response to the arguments is set forth.

2. Claims 3 and 6 have been cancelled

3. Claim 7 has been amended.

4. Claims 1, 2, 4, 5 and 7-11 are under examination.

Rejections Withdrawn

5. The rejection of claims 3, and 6-11, under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of amendments to the claims.

6. The rejection of claims 3, and 6-11under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule encoding an amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for just any isolated nucleic acid molecule encoding a polypeptide with *at least one conservative amino acid substitution* from about amino acids 1-1297 or about amino acids 2-1297 is withdrawn in view of amendments to the claims.

New Grounds of Rejections

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, 4, 5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule having the nucleic acid sequence consisting essentially of that set forth in SEQ ID NO:1 and an isolated nucleic acid molecule encoding the amino acid sequence consisting essentially of that set forth in SEQ ID NO:2, does not reasonably provide enablement for an isolated nucleic acid molecule having a nucleic acid sequence consisting essentially of that set forth in SEQ ID NO:1 and an isolated nucleic acid molecule encoding a amino acid sequence consisting essentially of that set forth in SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to an isolated nucleic acid molecule having a nucleic acid sequence consisting essentially of that set forth in SEQ ID NO:1 and an isolated nucleic acid molecule encoding a amino acid sequence consisting essentially of that set forth in SEQ ID NO:2. Thus the claims are broadly drawn to a nucleic acid comprising anywhere from two nucleic acids to the entire length of SEQ ID NO:1, because the claim 1 recites ".....nucleic acid molecule having a nucleic acids sequence.....". Similarly because claim 2 recites ".....nucleic acid molecule encoding an amino acid sequence.....", the claim can be interpreted a nucleic acid molecule that encodes

anywhere from two consecutive amino acids to the entire length of the amino acid sequence as set forth in SEQ ID NO:2.

Thus, the instant claims as interpreted broadly are not enabled because they read on only a part of the nucleic acid set forth in SEQ ID NO:1, and a nucleic acid molecule that encodes only a part of the amino acid sequence set forth in SEQ ID NO:2. Further, the claims also include a nucleic acid molecule that comprise any substitutions, insertions or deletions; because the claims as written comprise only apart of the nucleic acid sequence set forth in SEQ ID NO:1.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Even if one has the correct amino acid sequence, a skilled practitioner would not be able to predict the level of expression of the resulting

synthetic DNA sequence For example, the cellular location of the Int-2 oncoprotein is determined by the choice of initiation codon, i.e., either the AUG coding for methionine or CUG coding for leucine. AUG-initiated Int-2 proteins are secreted from the cells, while CUG-initiated Int-2 proteins are localized to the cell nucleus (Acland et al., Nature. 1990, Vol 343:662-665).

Although biotechnology has made great strides in the recent past, these references serve to demonstrate exactly how little we really know about the art. Elucidation off the genetic code induces one to believe that one can readily obtain a functional synthetic protein for any known nucleic acid sequence with predictable results. The results of the construction of synthetic proteins remain very unpredictable as the above-cited references conclusively demonstrate.

In addition, Ibragimova and Eade (Biophysical Journal, Oct 1999, Vol. 77, pp. 2191-2198) teach that factors affecting protein folding and stability are governed by many small and often opposing effects and that even when the "rules" are know for altering the stability of a protein fold by the introduction of a single point mutation the result is not reliable because the balance of forces governing folding differs for different protein sequences, and that the determination of the relative magnitude of the forces governing the folding and stability of a given protein sequence is not straightforward (page 2191, first column, lines 12-17 and second column, lines 3-8).

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to producing and using the myriad of derivatives encompassed in the scope of the claims, one skilled in the art would be forced into undue

experimentation in order to practice the broadly claimed invention.

Amending the claims such that ".....having a nucleic acid..." in line 1 of claim 1, and "....encoding an amino acid....." in line 1 of claim 2 are amended to ".....having the nucleic acid..." and "....encoding the amino acid.....", respectively would obviate the above rejection.

Please note that the attorney of recode, Mr. Paul Carango, was contacted in this regard who indicated that the best mode of action is an office action instead of an examiners amendment.

Conclusion

9. No claims are allowed

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi, Ph.D.
Ph: (571) 272-8789

SHEELA HUFF
PRIMARY EXAMINER